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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,447	09/01/1999	Sachdev S. Sidhu	P1581R2	2633

23552 7590 09/13/2006

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EXAMINER	
TRAN, MY CHAU T	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/380,447	SIDHU ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7-9,11,12,29-33,44-49 and 52-58* is/are pending in the application.

4a) Of the above claim(s) *29,48,49 and 52-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7-9,11,12,30-33,44-47 and 55-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 07/07/2006 are acknowledged and entered.

2. Claims 1, 3, 4, 7-9, 11, 12, 29-33, 44-49, and 52-58 were pending. Applicants have amended claims 3, 4 and 44. No claims were added and/or cancelled. Therefore, claims 1, 3, 4, 7-9, 11, 12, 29-33, 44-49, and 52-58 are currently pending.

Election/Restrictions

3. The instant species election requirement is still in effect as there is no allowable generic or linking claim. Applicant has elected the following species for the elected invention (Claims 1, 3, 4, 7-9, 11, 12, 29-33, 44-49, and 52-58) in the reply filed on 11/02/2004:

a. For the single specific species of a major coat protein, applicant elected a filamentous phage of gp VIII, i.e. wild type M13 with the sequence of SEQ ID NO. 2.

b. For the single specific species of variant of the major coat protein, applicant elected variant of the major coat protein, i.e. wild type M13 with the sequence of SEQ ID NO. 2, wherein the amino acid and its position are as follows: Position No./Amino Acid: 1/D, 2/K, 3/S, 4/E, 5/K, 6/F, 7/S, 8/R, 9/D, 11/Y, 12/E, 13/A, 14/L, 15/E, 16/D, 17/I, 18/I, 19/T, 20/N, 21/L, 22/F, 23/F, 24/L, 25/L, 26/G, 27/T, 28/V, 29/Y, 30/V.

c. For the single specific species of heterologous protein, applicant elected an antibody or fragment thereof.

d. For the single specific species of linking peptide, applicant elected SEQ ID NO. 110.

e. For the single specific species of target, applicant elected erb 2.

4. Claims 29, 48, 49, and 52-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***non-elected species***, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/2/2004.

5. Please note: Applicant's *specifically* elected species of a fusion protein, which comprises a variant of filamentous phage of gp VIII, i.e. wild type M13 with the sequence of SEQ ID NO. 2 wherein its amino acid variant at the following position are as follows: (Position No./Amino Acid) 1/D, 2/K, 3/S, 4/E, 5/K, 6/F, 7/S, 8/R, 9/D, 11/Y, 12/E, 13/A, 14/L, 15/E, 16/D, 17/I, 18/I, 19/T, 20/N, 21/L, 22/F, 23/F, 24/L, 25/L, 26/G, 27/T, 28/V, 29/Y, 30/V; a linking peptide of SEQ ID NO. 110; and an antibody that binds to erb 2 (see paragraph 6 above). The elected species of a fusion protein was searched and was not found in the prior art. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim.

Thus the search was expanded to non-elected species, which *were* found in the prior art; see rejections below.

6. Claims 1, 3, 4, 7-9, 11, 12, 30-33, 44-47, and 55-58 are under consideration in this Office Action.

Status of Claim(s) Objection(s) and /or Rejection(s)

7. The rejections of claims 3 and 44 under 35 USC 112, second paragraph, as being indefinite have been withdrawn in light of applicant's amendments of claims 3, 4, and 44.

Maintained Rejection(s)

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 3, 4, 7-9, 11, 12, 30-33, 44-47, and 55-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 1 recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7

phage. Claim 32 recites the limitation "*wherein the filamentous phage coat protein is a hyper-functional variant of the major coat protein that increases the number of fusion proteins incorporated into a virus particle*", i.e. a functional limitation of the instantly claimed variant of a wild type major coat protein of a filamentous phage. Claim 33 recites the limitation "*wherein the filamentous phage coat protein is a hyper-functional variant of the major coat protein that decreases the number of fusion proteins incorporated into a virus particle*", i.e. a functional limitation of the instantly claimed variant of a wild type major coat protein of a filamentous phage.

With regard to the written description requirement, the attention of the Applicant is directed *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985)(quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the

enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.* And also *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

In this case, the instant invention claimed a broad genus of a fusion protein that comprises a variant of a wild type major coat protein of a virus, which represents enormous scope because the claims do not place any limitations on the site of the mutation(s) (i.e. the substituting amino acid residues, substituting position(s), and the region/segment of substitution such the N-terminal, the hydrophobic transmembrane, or the DNA-binding segment) to form such a variant of a wild type major coat protein of a virus. Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of a virus. Although as claimed the virus includes a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, this limitation is not sufficient in describing the variety of species to reflect the variation within the genus of a variant of a wild type major coat protein of a virus. For example, Williams et al. disclose that within the subgenera of a wild type filamentous phage the coat proteins of M13 and IKe are structurally distinct from each other and have different hydrophobicity (see pg. 10480, right col., lines 47-58).

In addition, instant claimed variant of a wild type major coat protein of a filamentous phage is further define by a functional limitations of claims 32 and 33, i.e. the variant of a wild type major coat protein of a filamentous phage would increase (of claim 32) or decrease (of

claim 33) "*the number of fusion proteins incorporated into a virus particle*", which does not alleviate these deficiencies. The CFC has also stated that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials" (e.g., see University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)). Here, applicants have failed to provide a definition, structure, or formula for any of the instant claimed composition, i.e. the site of the mutation(s) such as the substituting amino acid residue(s), substituting position(s), and the region/segment of substitution such as the N-terminal, the hydrophobic transmembrane, or the DNA-binding segment, that would result in a variant with extreme variation in function, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*". In addition, the CAFC has stated that a genus, which is set forth only in functional term, "...is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function" (e.g. see University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997)). Applicants provide no chemical structure for the claimed genus of compounds, i.e. a variant of a wild type major coat protein of a virus, and only distinguish the claimed genus from others, except by function, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*". For example, while the structure features (i.e. sequences) of the wild type major coat protein of a virus, i.e. a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, are known in the prior art, and the methods for making a variant of a wild type major coat protein of a virus (i.e. randomized or saturation site

directed mutagenesis) are known at the time of filing such methods were not sufficiently routine or predictable at the time of filing, to permit one of skill in the art to devise strategies for making a variant of a wild type major coat protein of a virus that would result in a variant with extreme variation in function, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*". Williams et al. disclose that the Pro 30 mutants of IKe are less viable than the wild-type IKe (see pg. 10476, left col., lines 3-26; pg. 10476, fig. 3; pg. 10481, left col., lines 6-11). Moreover, Williams et al. disclose mutation in the same position in M13 coat protein result in either unsuccessful mutation or small residue substitution occurs (see pg. 10481, left col., lines 18-26 and 42-51), i.e. mutation among the species of the filamentous phage genera do not produce similar result or it is unsuccessful. As a consequence, the mutagenesis methodologies is known to be difficult to optimize such that a successful mutation can occur and/or producing a mutant with extreme variation in function as claimed in claims 32 and 33, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*".

Consequently, the claimed limitation of a variant of a wild type major coat protein of a virus represents a broad genus.

In contrast, the instant specification examples are drawn to the method of making the variant of wild type major coat protein VIII of the filamentous phage (see pgs. 72-74, Example 10-12; pgs. 80-83, Examples 24-25) and the method of using the variant of wild type major coat protein VIII of the filamentous phage (see pgs. 74-77, Example 13-21; pgs. 84-85, Example 26).

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22,

1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires ***representative examples***, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is ***substantial variation within the genus***, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, the instant specification has only provided working examples for only the variant of the wild type major coat protein VIII of the filamentous phage. Thus, a person of skill in the art would not believe that applicants were in possession of a genus that encompasses virtually an infinite number of compounds and/or compositions encompassing every class and subclass of the instant claimed a fusion protein that comprises a variant of a wild type major coat protein of a virus that includes a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

Accordingly, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. The instant specification and claims do not provide any guidance as to what changes should be made to extend the instant specification one example to the infinite number of possibilities that are currently being claimed compound, i.e. a variant of a wild type major coat protein of a virus that includes a filamentous phage, a lambda

phage, a Baculovirus, a T4 phage and a T7 phage, for the instant claimed a fusion protein. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, the instant specification single example is insufficient to describe the enormous genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach instant claimed fusion protein comprising a heterologous polypeptide and any variant of any wild type major coat protein of phage display systems that includes the display systems of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage. Therefore, only the fusion protein comprising a heterologous polypeptide and the variant of wild type major coat protein of a filamentous phage,

specifically the coat protein VIII, but not the full breadth of the claimed product meet the written description provision of 35 U.S.C 112, first paragraph.

Response to Arguments

10. Applicant's arguments directed to the above 112, first paragraph, rejection were considered but they are not persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicant's newly amended and/or added claims and/or arguments.

[1] Applicant contends that the instant specification need not identify any "core structure" of the wild type major coat proteins recited by the claims since the wild type major coat proteins are known in the art.

[2] Applicant alleges that the instant specification disclosures and the working examples the variant of the wild type major coat protein VIII of the filamentous phage are sufficient for the claimed genus of variant major coat protein.

This is not found persuasive for the following reasons:

[1] The examiner respectfully agrees that the instant specification need not identify any "core structure" of the wild type major coat proteins recited by the claims since the wild type major coat proteins are known in the art. However, while the structure features (i.e. sequences) of the wild type major coat protein of a virus, i.e. a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, are known in the prior art, and the methods for making a variant of a wild type major coat protein of a virus (i.e. randomized or saturation site directed mutagenesis) are known at the time of filing such methods were not sufficiently routine or predictable at the time of filing, to permit one of skill in the art to devise strategies for making a

variant of a wild type major coat protein of a virus that would result in a variant with extreme variation in function, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*" as discussed in the above rejection of paragraph 9.

[2] The examiner respectfully disagrees. It is the examiner's position that the instant specification disclosures and the working examples the variant of the wild type major coat protein VIII of the filamentous phage are insufficient for the claimed genus of variant major coat protein because Williams et al. disclose mutation in the same position in M13 coat protein result in either unsuccessful mutation or small residue substitution occurs (see pg. 10481, left col., lines 18-26 and 42-51), i.e. mutation among the species of the filamentous phage genera do not produce similar result or it is unsuccessful. As a consequence, the mutagenesis methodologies is known to be difficult to optimize such that a successful mutation can occur and/or producing a mutant with extreme variation in function as claimed in claims 32 and 33, i.e. increase (of claim 32) or decrease (of claim 33) "*the number of fusion proteins incorporated into a virus particle*". Consequently, the instant specification and claims do not provide any guidance as to what changes should be made to extend the instant specification one example, i.e. the variant of the wild type major coat protein VIII of the filamentous phage, to the infinite number of possibilities that are currently being claimed compound, i.e. a variant of a wild type major coat protein of a virus that includes a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, for the instant claimed a fusion protein.

Therefore, the specification does not teach instant claimed fusion protein comprising a heterologous polypeptide and any variant of any wild type major coat protein of phage display

systems that includes the display systems of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, and the rejection is maintained.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 8, 9, 11, 12, 30, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/1997*).

> *The instant invention recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.*

Larocca et al. disclose a genetic package display system and the method of using it (see e.g. Abstract; col. 2, lines 14-63; col. 3, lines 3-19). The genetic package display system comprises a ligand fused to the phage coat protein (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 57-65; fig. 1B). The ligand includes foreign protein, peptides, antibodies, or cDNA (refers to instant claimed heterologous polypeptide and instant claims 8, and 46)(see e.g. col. 4, line 64-65; col. 5, line 54 thru col. 6, line 62; col. 9, lines 57-65). In addition the ligand can bind to target such as erbB3 (refers to instant claim 47)(see e.g. col. 11, lines 18-30). The phage coat

protein comprises a wild type major coat protein such as filamentous phage, lambda phage, and T4 phage (refers to instant claim 30)(see e.g. col. 4, line 66 thru col. 5, line 53) or mutant coat protein such as the mutant filamentous phage coat protein VIII (refers to instant claimed variant of a wild type major coat protein of a virus and the elected species of filamentous phage of gp VIII)(see e.g. col. 9, lines 36-44). The transformation of the genetic package display system uses host cell such as bacteria host cell (refers to instant claims 9 and 11)(see e.g. col. 7, lines 15-22; col. 10, lines 46-63; col. 11, lines 1-17; col. 17, lines 1-31) and include viral replication system (refers to instant claim 12)(see e.g. col. 7, line 33 thru col. 8, line 6). Therefore, the genetic package display system of Larocca et al. anticipates the presently claimed fusion protein.

Response to Arguments

13. Applicant's arguments directed to the above 102(e) rejection were considered but they are not persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicant's newly amended and/or added claims and/or arguments.

[1] Applicant contends that the effective filing date of the present application, i.e. 10/08/1998, antedates the effective filing date of Larocca et al., i.e. 08/28/1998.

[2] Applicant alleges that Larocca et al. is not entitled to this priority date 08/28/1998 because priority application of 09/141,631 do not disclose a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

This is not found persuasive for the following reasons:

[1] The examiner respectfully disagrees. It is the examiner's position that the reference of Larocca et al. is given the priority of provisional application of 60/057,067 filed 08/29/1997, and as a result, the ***effective filing date*** Larocca et al. is 08/29/1997. Therefore, the effective filing date of the present application does not antedate the effective filing date of Larocca et al.

[2] The examiner respectfully disagrees. In response to applicant's argument that Larocca et al. is not entitled to this priority date 08/28/1998 because priority application of 09/141,631 do not disclose a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, this argument is moot since the reference of Larocca et al. is given the priority of provisional application of 60/057,067 filed 08/29/1997, and as a result, the ***effective filing date*** Larocca et al. is 08/29/1997.

Therefore, the genetic package display system of Larocca et al. anticipates the presently claimed fusion protein, and the rejection is maintained.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 7-9, 11, 12, 30-32, 46, 47, 55, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/199*) in view of Li et al. (*J. Biol. Chem.*, **1993**, 268(7), pgs. 4584-4587).

> *The instant invention recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.*

Larocca et al. disclose a genetic package display system and the method of using it (see e.g. Abstract; col. 2, lines 14-63; col. 3, lines 3-19). The genetic package display system comprises a ligand fused to the phage coat protein (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 57-65; fig. 1B). The ligand includes foreign protein, peptides, antibodies, or cDNA (refers to instant claimed heterologous polypeptide and instant claims 8, and 46)(see e.g. col. 4, line 64-65; col. 5, line 54 thru col. 6, line 62; col. 9, lines 57-65). In addition the ligand can bind to target such as erbB3 (refers to instant claim 47)(see e.g. col. 11, lines 18-30). The phage coat protein comprises a wild type major coat protein such as filamentous phage, lambda phage, and T4 phage (refers to instant claims 30 and 31)(see e.g. col. 4, line 66 thru col. 5, line 53) or mutant coat protein such as the mutant filamentous phage coat protein VIII (refers to instant claimed variant of a wild type major coat protein of a virus and the elected species of filamentous phage

of gp VIII)(see e.g. col. 9, lines 36-44). In addition, the mutant coat protein increases transduction efficiency (refers to instant claim 32)(see e.g. col. 9, lines 36-44; especially col. 9, lines 40-44). The transformation of the genetic package display system uses host cell such as bacteria host cell (refers to instant claims 9 and 11)(see e.g. col. 7, lines 15-22; col. 10, lines 46-63; col. 11, lines 1-17; col. 17, lines 1-31) and include viral replication system (refers to instant claim 12)(see e.g. col. 7, line 33 thru col. 8, line 6).

The fusion protein of Larocca et al. differs from the presently claimed invention by failing to disclose the amino acid substitution for the variant of a wild type major coat protein.

Li et al. disclose mutant M13 coat protein (see e.g. Abstract; pg. 4584, right col., lines 6-37; pg. 4585, fig. 1). The mutagenesis comprises randomized oligonucleotides annealed to either the wild type major coat protein of M13 or the mutant of the wild type major coat protein of M13 and the transformation step use *E coli* as the host cell (see e.g. pg. 4584, right col., lines 40-69; pg. 4585, left col., lines 8-19). The amino acid substitution ranges from 2 to 13 and the site of the mutation is at residues numbers 22, 23, 24, 27, 28, 29, 30, 31, 32, 33, 36, 37, and 38 (see e.g. pg. 4584, right col., line 40 thru pg. 4585, left col., line 6; pg. 4585, left col., lines 19-47; pg. 4585, fig. 1).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose the amino acid substitution for the variant of a wild type major coat protein as taught by Li et al. in the fusion protein of Larocca et al. One of ordinary skill in the art would have been motivated to disclose the amino acid substitution for the variant of a wild type major coat protein in the fusion protein of Larocca et al. for the advantage of providing a major coat protein with alter species distributions and protein-protein interaction within the

transmembrane region (Li: pg. 4586, right col., lines 5-11) since both Larocca et al. and Li et al. disclose mutant filamentous phage major coat protein VIII (Larocca: col. 9, lines 40-44; Li: pg. 4585, fig. 1). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Larocca et al. and Li et al. because Li et al. disclose the success of the amino acid substitution for the variant of a wild type major coat protein for use in mutagenesis (Li: pg. 4585, right col., lines 3-14).

Therefore, the combine teachings of Larocca et al. and Li et al. do render the fusion protein of the instant claims *prima facie* obvious.

Response to Arguments

17. Applicant's arguments directed to the above 103(a) rejection were considered but they are not persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicant's newly amended and/or added claims and/or arguments.

[1] Applicant contends that the combine teachings of Larocca et al. and Li et al. do not render the fusion protein of the instant claims *prima facie* obvious because the reference of Larocca et al. is not prior art against the present application for the effective filing date of the present application, i.e. 10/08/1998, antedates the effective filing date of Larocca et al.

[2] Applicant alleges that although Li et al. discloses mutant M13 major coat protein, the reference of Li et al. do not teach or suggest a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. Thus, the reference of Li et al. does not remedy the deficiency of the reference of Larocca et al.

This is not found persuasive for the following reasons:

[1] The examiner respectfully disagrees. It is the examiner's position that the reference of Larocca et al. is given the priority of provisional application of 60/057,067 filed 08/29/1997, and as a result, the ***effective filing date*** Larocca et al. is 08/29/1997. Therefore, the effective filing date of the present application does not antedate the effective filing date of Larocca et al., and the reference of Larocca et al. is prior art against the present application.

[2] The examiner respectfully disagrees. It is the examiner's position that although the reference of Li et al. do not teach or suggest a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus, the reference of Li et al. is not use to cure the deficiency of a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus since the reference of Larocca et al. is prior art against the present application. Moreover, the reference Larocca et al. does teach a fusion protein comprising a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 36-44 and 57-65; fig. 1B).

Consequently, the combine teachings of Larocca et al. and Li et al. do render the fusion protein of the instant claims *prima facie* obvious, and the rejection is maintained.

Status of Claim(s) Objection(s) and /or Rejection(s)

18. The rejection of claims 1, 7-9, 11, 12, 30-32, 46, 47, 55, and 58 under 35 USC 103(a) as being obvious over Light, II et al. (US Patent 5,770,356) in view of Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/1997*) has been withdrawn upon reconsideration of

the rejection that is view as being redundant since the reference of Larocca et al. is used as a 102 rejection to reject these claims.

Conclusion

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
September 5, 2006

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SUPERVISORY PATENT EXAMINER
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